Amendments to the Specification:

AMENDMENTS TO THE SPECIFICATION:

Please replace the paragraphs as shown below in order to address the objections to the specification concerning sequences:

On page 32 of the specification, please replace the second paragraph with the following replacement text:

RNA was prepared using the ~~RNeasy~~ RNEASY ® (RNA Extraction) kit from Qiagen, as described by the ~~manufactor~~ manufacturer (Qiagen, Hilden, Germany). RNA was prepared from patients with B-CLL without hyper mutation who, by PCR analysis, using primers FDP5 (CCTTTATGTGTGTGACAAGTG; SEQ ID No:29) and F10 (ATCCAGCCAGGATGAAATAGAA; SEQ ID No:30), showed a high level of the resulting PCR fragment. Poly-A^+ RNA was isolated from total RNA by the ~~"MicroPoly(A)Purist"~~ MICROPOLY(A)PURIST ® (RNA Purification) kit from Ambion, as described by the manufactor (Ambion, Inc., Texas, USA). Cloning-ready cDNA was prepared from 8 µg poly-A^+ RNA using the ~~"ZAP Express® XR Library Construction Kit"~~ ZAP EXPRESS® XR Library Construction Kit from Stratagene as described by the ~~manufactor~~ manufacturer (Stratagene, San Diego, USA). The cDNA was size fractionated and two size fractions (fraction-1: > 2500 bp and fraction-2 300-2500 bp) were independently ligated to pre-digested lambda Zap vectors and packed into phage particles as described by the ~~manufacture~~ manufacturer (Stratagene, San Diego, USA). The titer was determined for each library and 200,000 pfu of from the fraction-1 library were plated onto two 22x22 cm screening plates (100,000 pfu on each plate) and 750,000 pfu of the fraction-2 library were plated on five 22x22 cm screening plates (150,000 pfu on each) as described by Stratagene, San Diego, USA. The plates were incubated at 37°C for 18 hours and the plaques transferred to replica nylon filters (Amersham) and denatured and renatured to allow hybridisation. All procedures were made as described by the ~~manufactures~~ manufacturers (Stratagene, San Diego, USA & Amersham Biosciences, Buckinghamshire, UK).

On page 32 of the specification, please replace the third paragraph with the following replacement text:

The filters were screened by independent hybridisations with alpha[^{32}P]-dATP-labelled DNA fragments; alpha[^{32}P]-dATP was purchased from Amersham Biosciences, Buckinghamshire, UK. Between succesive hybridisations, the old probe was removed by incubation for 20 min in 2l 90-100°C water containing 0.1% SDS . The DNA fragments used as probes were (all positions relate to sequence ID # X): 1) pos. 48978-49250; 2) pos. 50011-51591; 3) pos. 51461-52182; 4) pos. 51901-52589; 5) pos. 53121-56521; 6) pos. 58163-59408. All hybridisations and washes were made according to the ~~indtructions~~ instructions from Stratagene, San Diego, USA and Amersham Biosciences, Buckinghamshire, UK; Washing was done at a high stringency (0.1 x SSC at 65°C for 20 min).

On page 33 of the specification, please replace the first paragraph with the following replacement text:

A total of 8 cDNAs were identified by cDNA cloning or by a combination of cDNA cloning, PCR analysis and RACE (rapid amplification fo cDNA ends-polymerase chain reaction) using the the SMART ™ RACE cDNA amplification kit (Clontech, Palo Alto, CA) according to the manufacturer's instructions.

On page 34 of the specification, please replace the paragraph immediately following the heading "Determination of somatic hypermutation status" with following replacement text:

Two µl of cDNA was amplified using a GeneAmp PCR System 2700 (Applied Biosystems, Warrington, UK) with a 40 pmol specific upstream primer corresponding to 1 of the 6 human VH family leader sequences (VH1 (SEQ ID No:31): 5'-CCATGGACTGGACCTGGAGG-3', VH2 (SEQ ID No:32): 5'-ATGGACATACTTTGTTCCAGC-3', VH3 (SEQ ID No:33): 5'-CCATGGAGTTTGGGCTGAGC-3', VH4 (SEQ ID No:34): 5'-

ATGAAACACCTGTGGTTCTT-3', VH5 (SEQ ID No:35): 5'-ATGGGGTCAACCGCGATCCT-3', VH6 (SEQ ID No:36): 5'-ATGTCTGTCTCCTTCCTCAT-3') and a 40 pmol downstream primer (Cμ (SEQ ID No:37):5'-GAGGCTCAGCGGGAAGACCTT-3' or Cγ (SEQ ID No:38):5'-GGGGAAGACCGATGGGCCCCT-3') corresponding to a consensus sequence of the constant region of IgM or IgG respectively. The Reverse Transcription (RT)-PCR reaction contained 1xPCR buffer (10mM Tris-HCl, pH 9.0, 50mM KCl, 0.1% Triton X-100), 2.5mM $MgCl_2$, 0.2mM of each dNTP and 1.5U Taq DNA Polymerase (Promega, Madison, WI, USA) in a final volume of 100μl. The RT-PCR was performed under the following conditions: 1 cycle of 94°C for 5 minutes, 30 cycles of denaturation at 94°C for 30 secs, annealing at 62°C for 30 sec. and extension at 72°C for 30 sec, and a final extension at 72°C for 7 minutes. The RT-PCR products were analysed on 2% agarose gels and sequenced in an HBI Prism 310 Genetic Analyzer (Perkin Elmer, Foster City ,CA, USA) using the BigDye Terminator Cycle Sequencing Ready Reaction kit (Applied Biosystems, Warrington, UK) following the manufacturer's instructions.

On page 35 of the specification, please replace the paragraph immediately following the heading "RT-PCR that amplifies the Exon 2-Exon 3 junction" with following replacement text:

To evaluate the mRNA expression pattern of AMB1 in unmutated and mutated B-CLL patients RT-PCR was performed. Exon-overlapping oligonucleotide primers were: 5'-ATCCAGCCAGGATGAAATAGAA-3' (SEQ ID No:30) and 5'-CACTTGTCACACACATAAAGG-3' (SEQ ID No:28). The RT-PCR was performed in a GeneAmp PCR System 2700 thermal cycler with an initial denaturation at 94°C for 2 minutes, 40 cycles of 96°C for 25 sec., 62°C for 25 sec. and 72°C for 90 secs, and a final extension at 72°C for 5 minutes. The reactions contained 2μl cDNA, 1x DDRT-PCR buffer (10mM Tris-HCl, pH 8.3, 50mM KCl, 1.8mM $MgCl_2$, 0.1% Triton X-100, 0.005% gelatine), 0.25mM of each dNTP, 30 pmol of each primer and 0.5U Taq DNA Polymerase (Promega, Madison, WI, USA) in a 30μl final volume. RT-PCR products were analyzed by gelelectrophoresis on 2% agarose gels and visualized with a Gene Genius Bio Imaging System (Syngene, Frederick, MD) after staining with ethidium

bromide. An actin control RT-PCR was performed using the primers: 5'-TGACGGGGTCACCCACACTGTGCCCATCTA-3' (SEQ ID NO: 42) and 5'-CTAGAAGCATTTGCGGTGGACGATGGAGGG-3' (SEQ ID NO: 43).

On page 35 of the specification, please replace the paragraph immediately following the heading "RT-PCR that amplifies the Exon 1-Exon 3 junction:" with following replacement text:

To evaluate the mRNA expression pattern of AMB1 in unmutated and mutated B-CLL patients RT-PCR was performed. Exon-overlapping oligonucleotide primers were: 5'-AGACGGCTCTCACC AATAAG-3' (SEQ ID No:27) and 5'-CACTTGTCACACACATAAAGG-3' (SEQ ID No:28). The RT-PCR was performed in a GeneAmp PCR System 2700 thermal cycler with an initial denaturation at 94°C for 2 minutes, 40 cycles of 96°C for 25 sec., 62°C for 25 sec. and 72°C for 90 secs, and a final extension at 72°C for 5 minutes. The reactions contained 2µl cDNA, 1x DDRT-PCR buffer (10mM Tris-HCl, pH 8.3, 50mM KCl, 1.8mM $MgCl_2$, 0.1% Triton X-100, 0.005% gelatine), 0.25mM of each dNTP, 30 pmol of each primer and 0.5U Taq DNA Polymerase (Promega, Madison, WI, USA) in a 30µl final volume. RT-PCR products were analyzed by gel electrophoresis on 2% agarose gels and visualized with a Gene Genius Bio Imaging System (Syngene, Frederick, MD) after staining with ethidium bromide (Continental Lab Products, San Diego, USA).

Please replace the paragraph spanning pages 35-36 of the specification with following replacement text:

Northern blotting. RNA from spleen, bone marrow and colon was purchased from Clontech. The AMB1 probe was an 896 base pair fragment (57661-56766) obtained by RT-PCR as described above with the primers 5'-TCACCTGGGAGCTCAGAGGA-3' (SEQ ID No:39) and 5'-GTGATCCTGGGAGAATCTCT-3' (SEQ ID No:40). For Northern blotting, 5 µg of RNA was run on a 1% agarose-gel with 6% formaldehyde dissolved in 1 x MOPS (20 mM 3-(N-morpholino)- propane-sulfonic acid, 5 mM sodium acetate, 1 mM EDTA, pH 7.0) for size separation. The presence of equal amounts of RNA in each lane

was ensured by ethidium bromide staining. The RNA was transferred to a Hybond-N membrane (Amersham, Little Chalfont, UK) by capillary blotting and fixed by UV-irradiation. The filters were pre-hybridized for 1-2 hours at 42°C in 6 ml ULTRAhyb (Ambion, Austin, TX, USA) preheated to 68°C and hybridized overnight at 42°C after addition of further 4 ml containing the ^{32}P-labeled probe and sheared salmon sperm DNA (10 µg/ml). The membranes were washed for 2 x 15 min. at 42°C in 2 x SSC, 0.1% SDS followed by 1 x 15 min. in 0.2 x SSC, 0.1 % SDS and 2 x 15 min. in 0.1 x SSC, 0.1 % SDS at 42°C. The blot was developed and quantified by a phosphoimager. The sizes of the mRNAs were determined by reference to 18S and 28S ribosomal RNA, which were visualized by ethidium bromide staining. The AMB1 probe used for hybridization was radiolabeled with [α-^{32}P] dCTP using the Random Primers DNA Labeling System (Gibco BRL).

On page 39 of the specification, please replace the paragraph immediately following the heading "Production of polyclonal antibodies:" with following replacement text:

Synthetic peptides CDLETNSEINKLIIYLFSQNNRIRF (SEQ ID NO: 44) and CQVSKKHIIYSTFLSKNF (SEQ ID NO: 45) were synthesized and conjugated to KLH (K.J.Ross-Petersen Aps, Holte, Denmark). Polyclonal antibodies were produced by immunization of rabbits with these conjugated peptides by DAKO (DAKO Cytomation A/S, Glostrup, Denmark).

On page 41 of the specification, immediately preceding the heading "References" please insert the following paragraph:

The sequence listing in the file named "10535500 (55320.001041).TXT" having a size of 179103 bytes and created April 17, 2008 is hereby incorporated by reference in its entirety.